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MILLEN,WHITE,ZELANO & BRANIGAN, P.C.
2200 Clarendon Blvd, Suite 1400
Arlington, VA 22201

EXAMINER
SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/027,439	PORTUGAL ET AL.	
	Examiner	Art Unit	
	Jehanne E Souaya	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *21 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-36,47,48 and 52-58* is/are pending in the application.

4a) Of the above claim(s) *21-36* is/are withdrawn from consideration.

5)☒ Claim(s) *52* is/are allowed.

6)☒ Claim(s) *47,48 and 53-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Currently, claims 21-36, 47, 48, 52, and newly added claims 53-58 are pending in the instant application. Claims 21-36 are withdrawn from consideration as directed to a non elected invention. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance.

Rejections in the previous office action applied to claims 37-39, 45, 46, and 49-51 are moot in view of cancellation of these claims. Applicant's amendment has rendered moot the rejections made in the previous office action under 35 USC 112/first paragraph.

Applicant's amendment necessitated the following rejections. These rejections are either newly applied or are reiterated (but newly applied to the amended and/or newly added claims, and thus are placed under the section heading "New Grounds of Objection and Rejection"). They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

Specification

2. The disclosure is objected to because of the following: Table 2, which was amended January 21, 1999, lists sequences that have not been identified by SEQ ID NO. Each entry in the table is required to be identified by a SEQ ID NO, even if some of the entries have identical SEQ ID NOS. For example, the fourth entry in the table does not have a SEQ ID NO. Although it is identical to SEQ ID NO 23, it should be identified by SEQ ID NO 23 as well. See 37 CFR1.821(d), MPEP section 2422. Appropriate correction is required.

Response to Arguments

The response states that since the claims do not refer to sequence in Table 2 of the specification, therefore there is no need to identify every entry in Table 2 by a SEQ ID NO. This argument was not found persuasive. MPEP section 2422.03 states "37 CFR 1.821(d) requires the use of the assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims" (9th para).

New Grounds of Objection and Rejection

Claim Objections

3. Claim 58 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 56 recites the limitation "a probe… consisting of a fragment greater than 10-40 bases in length of a nucleotide sequence of SEQ ID NO 3" which, for this particular recitation, appears to mean that the probe is no longer than SEQ ID NO 3 and contains only fragments from SEQ ID NO 3, however, claim 58 recites "a probe… which *comprises* 15-25 bases in length". Such recitation not only encompasses probes longer than SEQ ID NO 3, but also encompasses sequences on either side of the 15-25 bases that are not from SEQ ID NO 3, which are embodiments that do not necessarily further limit claim 56.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 55-58 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Newly added claims 55-58, as written, do not sufficiently distinguish over nucleic acids as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

Response to Arguments

The response asserts that claims 55-58 are drawn to fragments of sequences which have not been shown to exist in nature and that therefore it is not necessary to claim them as isolated molecules. This argument has been thoroughly reviewed but was not found persuasive as the claims are drawn to probes "comprising" fragments, and not just to the fragments themselves. With regard to claim 56, the recitation of "complementary" has no length limitation. Further, the definition for "probe" given in the specification is (see p. 17, lines 10-11) " a synthetic *or biologically produced* nucleic acid..."; which does not distinguish the term "probe" from a naturally occurring molecule as it can be 'biologically produced'.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 55-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Newly added claims 55 and 56 recite the limitation "greater than 10 to 40 bases in length". Such recitation is indefinite because it is unclear if a nucleic acid of 15 (for example, recited in claims 57 and 58) bases in length would meet the limitation of the claims as such is less than 40 bases. Consequently, the metes and bounds of the claims are unclear.

The recitation of "said molecule" in claims 55 and 56 lacks sufficient antecedent basis. The claims are drawn to a "probe" and do not recite the word molecule, therefore it is unclear if the recitation of "complementary to said molecule" refers to a nucleic acid that is complementary to the probe, or just to the fragment that the probe comprises.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for

patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 47, 48, 53, and 55-58 are rejected under 35 U.S.C. 102(a) and 102 (e) as being anticipated by Hogan (US Patent 5,541,308: 102(a) date -July 30, 1996; 102(e) date – 12/9/1988).

Instantly claimed SEQ ID NOS 3-6 are rRNA sequences of *Shigella flexneri, sonnei, dysenteriae, and boydii*, respectively.

Hogan teaches a probe which detects *E. coli* (see col. 52, line 17) (hereinafter termed "Sequence A") which is completely complementary to positions 991-120 of SEQ ID NO 3, and positions 989-1018 of SEQ ID NO 6. Sequence A of Hogan also has complementary sequences to both SEQ ID NO 4, over positions 990-1019, and SEQ ID NO 5 over positions 990-1019. Hogan teaches another sequence (see col. 52, lines 24-25) (hereinafter termed "Sequence B") which is completely complementary to positions 955-993 of SEQ ID NO 3, positions 954-992 of SEQ ID NO 5, and positions 953-991 of SEQ ID NO 6. With regard to positions 955-992 of SEQ ID NO 4, position 36 of the complement of Sequence B taught by Hogan contains a mismatch with position 958 of SEQ ID NO 4 and position 22 of the complement of Sequence B taught by Hogan contains an insertion between positions 971 and 972 of SEQ ID NO 4.

With regard to amended claims 47, 48, and newly added claims 53, and 55-58, Sequences A and B taught by Hogan are "capable of base pairing to SEQ ID NOS 3-6" according to the standard Watson Crick complementarity rules" (no conditions are specified in the claim). This recitation is not considered to limit the claimed nucleic acid to completely complementary sequences or full complements of SEQ ID NOS 3-6. With regard to claims 55 and 56, Sequence

A taught by Hogan is 30 bases, and Sequence B taught by Hogan is 39 bases, and therefore these sequences are "greater than 10 bases" in length. With regard to claims 57 and 58, the sequences taught by Hogan "comprises" 15-25 bases.

With regard to amended claims 47 and 48, sequence A taught by Hogan is capable of hybridizing to SEQ ID NOS 3 and 6, and sequence B taught by Hogan is capable of hybridizing to SEQ ID NOS 3, 5, and 6 under the conditions specified as they are completely complementary to sequences within SEQ ID NOS 3, 5, and 6. Further, with regard to the recitation of "targets" in claims 55 and 56, this term is broadly interpreted to encompass probes which will hybridize to or detect species of *Shigella*, which are considered inherent properties of the sequences taught by Hogan as Hogan teaches that Sequence A reacts with *Shigella* species (see col. 52, lines 47-49, and table 54), and the sequences are completely complementary to sequences within SEQ ID NOS 3, 5, and 6 and would hybridize to and detect SEQ ID NOS 3, 5, and 6.

9. Claim 54 is rejected under 35 U.S.C. 102(b) as being anticipated by Brennan et al (US Patent 5,474,796, 12/12/1995).

Brennan teaches oligonucleotide trimers, such as AGA (see Figure 1b), which meets the limitation of newly added claim 54, of an isolated nucleic acid molecule consisting of "a" nucleotide sequence of any of SEQ ID NOS 3-6. AGA are the first 3 nucleotides of SEQ ID NO 4. This rejection can be easily overcome by reciting instead "an isolated nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6 or an RNA equivalent thereof.

10. Claims 47, 48, 53, and 55-58 are rejected under 35 U.S.C. 102(a) as being anticipated by (in the alternative) Genbank accession numbers X96964 (4/4/96), or X80726 (3/29/1996, disclosed in Cilia et al 2/20/1996).

Instantly claimed SEQ ID NOS 4 is an rRNA gene sequence of *Shigella sonnei*.

Accession numbers X96964, and X80726 teach rRNA gene sequences of *Shigella sonnei*. (It is noted that sequence alignments with the claimed sequences are provided):

With regard to amended claims 47, 48, and newly added claims 53, and 55-56, the complements of the accession numbers are "capable of base pairing to SEQ ID NOS 4 according to the standard Watson Crick complementarity rules" (no conditions are specified in the claim). This recitation is not considered to limit the claimed nucleic acid to completely complementary sequences or the full complement of SEQ ID NOS 4. Additionally, with regard to claim 55, accession number X96964 is 1488 base pairs and accession number X80679 is 1467 base pairs. Such sequences comprise a fragment "greater than 10 bases to 40 bases of SEQ ID NO 4". With regard to claims 57 and 58, the accession numbers "comprises" 15-25 base pairs. Further, as these sequences are rRNA sequence of *Shigella sonnei*, the complements of such would necessarily "target" *Shigella sonnei*.

Also, with regard to amended claims 47 and 48, the complements of the accession numbers are considered "substantially complementary" to the claimed SEQ ID NO and would be capable of hybridizing to the SEQ ID NO under the recited conditions. The recitation of "substantially complementary... capable of hybridizing" to the nucleic acid molecule is not sufficient to distinguish the claimed nucleic acids from the complement of the accession numbers. Firstly, the claim's amended recitation of "substantially complementary" necessarily

stipulates that such sequences are not necessarily fully complementary or complete complements of the recited SEQ ID NOS. Secondly, the specification teaches at page 17, that such conditions could tolerate mismatches, and further at page 33, "the effect of a one base mismatch is decreased with a longer probe". SEQ ID NO 4 and accession number X96964 contain 5 mismatches. The complement of the accession number would hybridize to SEQ ID NO 4 because the effect of the 5 mismatches would be diminished due to the length of the accession number (1488 base pairs). SEQ ID NO 4 and accession number X80726 contain 10 mismatches. The complement of the accession number would hybridize to SEQ ID NO 4 because the effect of the 10 mismatches would be diminished due to the length of the accession number (1467 base pairs).

Note: the accession numbers teach the 16S rRNA "gene" (see "Definition") which is considered double stranded. Although the accession numbers do not specifically recite the complement, such is considered an inherent teaching of a "gene".

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 47, 48, 53, and 55-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Accession number A14565 (September 29, 1994) in view of Dyson, N.J. (Essential Molecular Biology Vol. II: A Practical Approach, chapter 5, pages 111-156, Brown, T.A. ed. Oxford University Press, Oxford, 1992).

Accession number A14565 teaches a sequence of 16S rRNA from E. Coli.

With regard to amended claims 47, 48, and newly added claims 53, and 55-56, the complement of the accession number is "capable of base pairing to SEQ ID NO 3 according to the standard Watson Crick complementarity rules" (no conditions are specified in the claim). This recitation is not considered to limit the claimed nucleic acid to completely complementary sequences or the full complement of SEQ ID NOS 3. Additionally, with regard to claim 55, the accession number is 1541 base pairs. Such sequence comprises a fragment "greater than 10 bases to 40 bases of SEQ ID NO 3". With regard to claims 57 and 58, the accession number "comprises" 15-25 base pairs. With regard to the recitation of "targets *Shigella flexneri*", (claims 55 and 56) such recitation is broadly interpreted to encompass sequences that could hybridize to *Shigella flexneri* (see paragraph below).

Also, with respect to amended claims 47 and 48, the complement of the accession number is considered "substantially complementary" to the claimed SEQ ID NOS and would be

capable of hybridizing to the SEQ ID NOS under the recited conditions. The recitation of "substantially complementary... capable of hybridizing" to the nucleic acid molecule is not sufficient to distinguish the claimed nucleic acids from the complement of the accession numbers. Firstly, the claim's amended recitation of "substantially complementary" necessarily stipulates that such sequences are not necessarily fully complementary or complete complements of the recited SEQ ID NOS. Secondly, the specification teaches at page 17, that such conditions could tolerate mismatches, and further at page 33, "the effect of a one base mismatch is decreased with a longer probe". The sequence of accession number A14565 contains only 5 mismatches and a gap of 1 nucleotide with respect to the entirety of SEQ ID NO 3 (sequence alignment provided). The complement of the accession number would hybridize to SEQ ID NO 3 because the effect of the 4 mismatches would be diminished due to the length of the accession number (1541 base pairs).

Although accession number A14565 does not teach the full complement of the sequence, it would have been prima facie obvious to one of ordinary skill in the art to construct the full complement of accession number A14565 to obtain a probe that would hybridize to accession number A14565 for the purposes of detecting accession number A14565. Such methods were readily used in the art at the time of the invention, as exemplified by Dyson, which teaches constructing probes for the purposes of hybridization detection assays..

Response to Arguments

With regard to prior art rejections, the response asserts that since SEQ ID NOS 3-6 are free of any cited prior art, that complementary sequences, substantially complementary sequences, and fragments thereof above 10-40 bases is novel and unobvious. This argument was

not found persuasive because the amended claim recitations encompass sequences disclosed in the prior art for the detailed reasons explained above. Further, the amended recitation of "complementary ... capable of base pairing according to the standard Watson-Crick complementarity rules", while encompassing complete complements, also encompasses sequences that contain mismatches with the claimed SEQ ID NOS as such would still be "capable of base pairing according to the standard Watson-Crick complementarity rules".

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Anderson (Gene probes 2, "Hybridization strategy", pp 1-29; Oxford University

Press, New York, Hames and Higgens Eds. 1995) which teaches hybridization strategies for using probes in hybridization detection assays, including such factors as length of probe, base composition, salt concentration, temperature, and discrimination between related sequences. Hammond (US Patent 5, 714,321) which teaches distinguishing C. pneumoniae from its closely related phylogenetic neighbors using probes specific for C. pneumoniae, and generally teaches probe design by sequencing and aligning sequences to maximize homology for the purposes of designing probes that will distinguish the sequences.

16. Claim 52 is allowable. Claims 47, 48, and 53-58 are not allowable over the cited prior art. SEQ ID NOS 3-6 are free of the cited prior art.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya
Patent examiner
Art Unit 1634

Jehanne Souaya
4/29/03